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Lemierre syndrome caused by *Leptotrichia buccalis* in a neutropenic patient

In 1936, Andre Lemierre, a French microbiologist, described a syndrome of internal jugular vein thrombophlebitis occurring during the course of anaerobic septicemia.[1] This condition, affecting young adults, began with post-anginal sepsis and progressed to metastatic septic emboli, frequently resulting in the death of the patient.

Most cases begin with oropharyngeal infection, although primary odontogenic infection, mastoiditis, sinusitis, and otitis media are occasionally the initial presentations.[2] Before the introduction of antibiotics, this syndrome had a fatal course. Nowadays, mortality is dramatically reduced by treatment with penicillin and other antibiotics.

Lemierre syndrome is usually caused by *Fusobacterium necrophorum* or *Fusobacterium nucleatum*, pleomorphic, anaerobic, Gram-negative bacilli.[3] However, patients with the primary focus in the oropharynx have polymicrobial septicemia. The concomitant bacteria are mostly oropharyngeal bacteria such as Peptostreptococcus, microaerophilic streptococci, and beta-hemolytic streptococci groups A, B and C. We report and discuss herein a case of post-anginal sepsis due to *Leptotrichia buccalis*.

The patient was a 21-year-old woman with a past medical history of autoimmune hepatitis. She was admitted to our unit for fever of unknown origin and was receiving azathioprine, 50 mg, twice daily. Because of a two point homozygous mutation in the thiopurine methyltransferase, she presented with neutropenia. The disease started with a fever, rigor, sweats, left-sided neck swelling, and a sore throat. On presentation, the patient had scleral icterus and was obviously uncomfortable. Vital signs included a temperature of 39.5 °C, a supine blood pressure of 85/50 mmHg, a regular pulse of 125 beats/min, and a respiratory rate of 30 breaths/min. Oral examination demonstrated erythema and swelling of the posterior pharyngeal mucosa and tonsils and ulcerative pharyngitis, with a fetid odor. Examination revealed swelling, warmth, and tenderness in the right side of the neck, without lymphadenopathy. Multiple non-tender posterior cervical lymph nodes were palpable on the right side of the neck. The lungs were clear on auscultation; pleural rub was not heard. However the patient complained of dyspnea. Cardiac exam results were significant for tachycardia, but no murmurs or gallops were detected by auscultation. Abdominal exam results were negative for tenderness and for hepatosplenomegaly. The skin showed no rashes or purpura. A neurologic examination was normal.

Laboratory tests revealed leukocytopenia (2.7×10^9/l), neutropenia (0.6×10^9/l), anemia (hemoglobin 58 g/l), and thrombocytopenia (platelets 21×10^9/l). There were no signs of disseminated intravascular coagulation. Other abnormal laboratory values were sodium 124 mmol/l, urea 9.9 mmol/l, bilirubin 25 μmol/l, albumin 25 g/l, SGOT 125 IU/l, and SGPT 158 IU/l. These investigations revealed a raised C-reactive protein (24 mg/dl). Specimens for an HIV enzyme-linked immunoassay, a monospot, and hepatitis C and B virus serology were drawn; results were negative. Urine was normal-colored with 2+ protein. Urine culture was sterile. Ultrasonography and Doppler ultrasound exploration of the neck showed jugular vein thrombosis. There were no signs of retropharyngeal abscess formation. A chest X-ray revealed multiple nodular infiltrates in both lungs. A contrast-enhanced computerized tomography (CT) scan of the chest suggested septic emboli as well as right basilar pneumonia. This CT scan of the chest showed solitary abscesses in the lungs and pleural effusion (Figure 1).

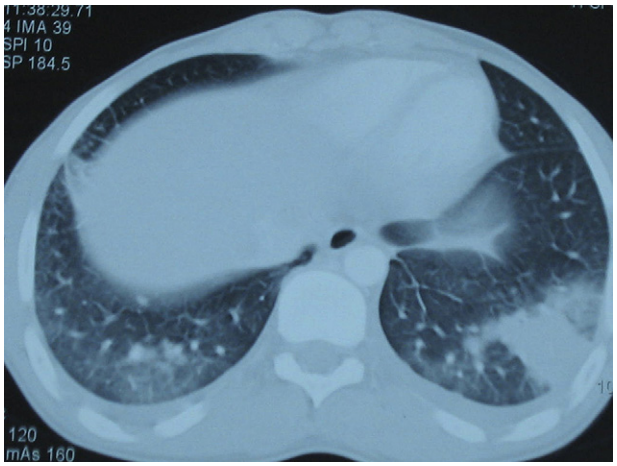

Figure 1 CT scan of the chest demonstrating right-side poster-obasal fluid. Both lungs show several hypodense areas, suspect abscesses, with consolidated lung tissue. There are no signs of pathology of the mediastinal region.

Treatment was started with intravenous broad-range antibiotics including ceftriaxone and metronidazole, fluids, and antipyretic drugs. Because a post-anginal complication was suspected and because of acute neutropenia, she was given high-dose intravenous piperacillin—tazobactam (12 g daily), ciprofloxacin (400 mg twice daily), and amikacin (15/mg/kg once daily for 2 days). On the third day of hospitalization, an anaerobic Gram-negative rod was isolated from serial blood cultures (two samples). Three days later, the species was identified as *L. buccalis*. Metronidazole was added, and amikacin was stopped. The patient improved clinically one week after the beginning of treatment. The patient was discharged from hospital on day 65. On review 12 weeks after discharge, there was general asthenia but general improvement.

We have described a new case of Lemierre syndrome, with internal jugular vein septic thrombophlebitis, septicemia, and multiple septic pulmonary emboli following a pharyngotonsillar infection.[2] There was no consensus on the diagnostic criteria. If we compare our patient to those described in the series of Lemierre, we can say that this patient has a Lemierre syndrome. However, our case remains atypical for many reasons: firstly our patient received immunosuppressive therapy and has an underlying liver disease, whereas the majority of patients with post-anginal sepsis are previously healthy. Moreover, our patient was neutropenic, and post-anginal sepsis is rarely described in this population. We did not find any other case of Lemierre syndrome with neutropenia. Secondly, even though the lung involvement remains compatible with a diagnosis of septic pulmonary emboli, we cannot confirm this diagnosis. Of particular interest in our case is the fact that the sole organism isolated was *L. buccalis*. The fact that it was isolated in more than one blood culture argues in favor of it being relevant pathogenically.

Leptotrichia spp are typically large, fusiform-shaped, non-sporulating, and non-motile rods.[4] More recently, based upon 16S rRNA sequencing, the genus *Leptotrichia* is believed to be one of the six genera in the family *Fusobacteriaceae* in the phylum *Fusobacteria*.[4] The primary habitat of *L. buccalis* is most likely the human oral cavity, typically dental plaque. As with the other oral flora, isolation of *L. buccalis* from these sites might be indicative of its role in periodontal disease or oral cavity abscesses.[5] Systemic infections are infrequent and mostly confined to patients with hematological malignancies and bone marrow transplant recipients, with neutropenia being the common underlying factor.[6] Because of its recent classification as a *Fusobacterium spp*, we think that there should be awareness of the possibility of Lemierre syndrome in patients with Leptotrichia bacteremia.

It remains difficult to link the clinical features of our patient and the sole *L. buccalis*. Given the fact that the origin of the infection remains the tonsils in our case, where mixed anaerobes are the rule, it is possible to detect secondary organisms as incidental findings that have leaked into the bloodstream. Indeed, in a significant proportion of cases in which *F. necrophorum* is isolated, other organisms are found. It is rare in the cases of classical Lemierre syndrome. In our case, we cannot exclude the possibility of *F. necrophorum* infection. Indeed, *F. necrophorum* could have been present in our patient, but undetected. A PCR study of a typical case of Lemierre syndrome in which cultures were negative detected *F. necrophorum* DNA.[7] This observation raises the possibility that this may be the cause in other culture-negative cases or even cases with organisms other than *Fusobacterium spp* isolated. We cannot exclude the possibility of concomitant bacteria such as *Fusobacterium spp* even though it was not detected. In our case, we did not perform PCR on a blood sample to prove infection with Fusobacterium.

In summary, *L. buccalis* bacteremia, although uncommon, could be associated with post-anginal sepsis. This syndrome should be kept in mind, and CT scans of the neck or Doppler ultrasound should be performed to assess the diagnosis of venous jugular thrombosis.

Conflict of interest: No conflict of interest to declare.

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Ganciclovir therapy in an immunocompetent child with resistant fever and hepatosplenomegaly due to cytomegalovirus infection. Who and when to treat?

Primary cytomegalovirus (CMV) infections in immunocompetent humans are self-limited infections from which patients generally recover without any medical intervention.[1,2] However, CMV infections can be seen with various clinical presentations in newborns. CMV is the most common congenital viral infection, occurring in 0.4—2.3% of all live births, and is probably a common cause of mental retardation and non-hereditary sensorineural deafness in children.[3]

Postnatally-acquired CMV infection in immunocompetent patients is generally subclinical but may sometimes give rise to a mild and self-limited mononucleosis-like syndrome.[4] The occurrence of CMV disease in transplant recipients and patients with AIDS is well described. CMV can cause severe pneumonitis, hepatitis, chorioretinitis, iridocyclitis, and pancreatitis with possible life-threatening multi-organ manifestations in immunocompromised persons.[5—7] We present herein the case of a 30-month-old immunocompetent girl with severe CMV infection with multiple organ involvement, who was successfully treated with ganciclovir.

A previously healthy 30-month-old girl was admitted to our hospital with fever, diarrhea, and abdominal distention of three-month duration. She was born of a healthy mother at 39 weeks of gestation (birth weight 2800 g) and had been breastfed for 4 months; at the age of 21 months, she had started attending a daycare center. Her temperature on admission was 38.5 °C, her heart rate was 110 beats per minute, and her blood pressure was 100/60 mmHg. Physical examination